

SUBJECT:

STRUCTURE AND FUNCTION OF THE NERVOUS SYSTEM

CREDITS:

Total:

10

Theory:

6

Practical:

4

GENERAL OBJECTIVE

The general objective of this subject is for students to acquire a basic knowledge of the structural, molecular and functional aspects of the mechanisms that control the working of the nervous system, the skin and the senses. This basic knowledge will allow students at a later stage to understand the biological foundations of pathology and therapeutics.

SPECIFIC OBJECTIVES

- Understand the molecular, cellular and electrophysiological bases of synaptic neurotransmission.
- Recognize the different elements that form part of the skin and its annexes.
- Understand the structural and functional bases of receptors and the transduction of sensory stimuli: mechanic, visual, auditory, gustatory and olfactory.
- Understand the organization and function of the motor system, from the cerebral cortex to the spinal medulla.
- Understand the structural and neurochemical organization of the different areas of the brain stem and their functional implications
- Integrate the coordination of motor activity carried out by the basal ganglia and the cerebellum.
- Learn the integrating purpose of the thalamus in the different functions of the nervous system
- Understand the structures involved in controlling limbic and autonomic functions.
- Understand the organizational models of the cerebral cortex and superior cognitive functions
- Learn the molecular and cellular bases of axonal growth and synaptic plasticity and apply them to pathological processes

PROGRAMME

Theory

I. INTRODUCTION

1. **Organization of the nervous system.** Nerve circuits and systems. Integration and plasticity. Functions of the Nervous System.

II. STRUCTURE, DEVELOPMENT, PROPERTIES AND FUNCTIONS OF NERVE CELLS

2. **Revision of the structure of cells that make up the nervous system.** Structure of the neuron: The cell body, dendrites and the axon. Types of neurons. Structure of nerve fibres and peripheral nerves. Neuroglial cells. Growth, survival and differentiation of neurons: Neural precursor cells. Cell proliferation. Neuron induction. Cell migration. Neuronal death during development.
3. **Electrical properties of neurons:** Capacitance, transference of charge and Ohm's Law Passive properties of the plasmic membrane. Membrane potential. Ionic equilibria and Nernst potential. Resting potential. Intracellular recording of electrical potential. Types and distribution of electrical conductivity. Action potential. Ionic mechanisms of action potential. Refractory periods. The frequency code. Generation and propagation of

action potentials. Speed of conduction of nerve fibres. Neuron response to stimulation. Different forms of neuronal electrical activity.

4. **Ion channels and membrane currents:** General characteristics and basic concepts. Types of ion channels. Methods of study: *Voltage-clamp* and *Current-clamp*, recording of single ion channels (*patch-clamp*). Ligand-regulated channels and voltage-regulated channels. Regulation of membrane ionic permeability. Creation and maintenance of ion gradients by ion pumps. Modulation of ion channels. Combinations of ionic currents are the basis of neuronal electrical activity.

III. COMMUNICATION BETWEEN NEURONS: THE SYNAPSE

5. **Types of synapse.** Electrical synapses and chemical synapses. Structure of synapses. The neuromuscular synapse: Mechanisms of neuromuscular transmission. Neuromuscular transmission disorders. The motor unit: concept.
6. **Neurotransmitter secretion:** Transport of neurotransmitters and their precursors. Quantal neurotransmitter secretion: The role of calcium in neurotransmitter secretion. The synaptic vesicle. Exocytosis. Molecular mechanisms of neurotransmitter exocytosis. Inhibition of exocytosis by specific toxins.
7. **Neurotransmitters:** definition, structure and types of action. Biosynthesis, Precursors. Systems of inactivation, degradation and reuptake of neurotransmitters. The different neurotransmitters: Acetylcholine, Monoamines, Amino Acids, Peptides, Nucleotides and Nitric Oxide.
8. **Receptors and transduction mechanisms:** Molecular and functional characteristics of neurotransmitter receptors. Types of receptors: Receptors directly coupled to an ion channel. Receptors indirectly coupled to ion channels. Second messengers. Neuromodulation. Molecular bases of neuromodulation.
9. **Electrophysiological aspects of synaptic transmission:** Excitatory and inhibitory postsynaptic potential: ionic bases. Effects of the passive properties of the membrane in synaptic transmission. Presynaptic and postsynaptic inhibition. Electrical neuromodulation: mechanisms that induce changes in the electrical behaviour of neurons.

IV. THE TEGUMENTARY SYSTEM: THE HUMAN SKIN

10. **General structure of the skin.** Embryological origin of its components. Regional variations. Dermatoglyphs.
The epidermis: Fine structure of the epidermis. Epidermopoiesis. Factors that regulate epidermopoiesis. The keratinocyte and its differentiation. Keratin. Filaggrin. The corneal layer. Lipid synthesis. Desmosomes. Keratinization and the development of epidermal keratins.
11. **Melanocytes.** Melanins and melanogenesis. Langerhans' cells. Merkel cells.
The dermis: Components of the dermis. Basic substance. Collagenase. Elastic tissue. Fibroblasts. Mastocytes and basophils in the dermis. The hypodermis.
12. **The dermoepidermal junction.** Ultrastructure. Components of the epidermal basal membrane. Localization of nerves and sensory terminals. Blood and lymphatic irrigation of the skin.
Skin annexes: The pilosebaceous apparatus. Pilose follicles. Structure of hair. Sebaceous glands, apocrine sweat glands and hair erector muscle. Eccrine sweat glands. Modified sweat glands. Ceruminous glands and Moll's glands. Nail structure. Histogenesis of the skin and its annexes.
13. **Functions of the skin:** The skin as a barrier. Mechanical functions. Immunity functions. Sensory functions. Sociosexual communication. Synthesis of vitamin D. Temperature regulation. Respiration.

V. ORGANIZATION AND FUNCTION OF THE SENSORY SYSTEM

14. **Somatosensory system.** Cutaneous touch receptors: Free nerve endings. Meissner's corpuscles. Merkel complexes or discs. Terminal organ of hair. Ruffini endings. Pacini corpuscles. Krause's end-bulbs. Subcutaneous Golgi-Mazzoni corpuscles.
Propioceptive receptors: The nerve endings of joints. The nerve endings of tendons. Sensitive innervation of striated muscle, neuromuscular fuses. The nerve endings in connective tissue. Visceral receptors: the nerve endings in visceral connective tissue. The nerve endings in smooth muscle. Nerve endings in cardiac muscle. Baroreceptors. Chemoreceptors. Ascending sensory pathways.
15. **The general problem of sensation.** Encoding and processing of sensory information. Sensory information as a basis of motor control, conscience and feelings. Feelings and perceptions. Sensory receptors: classification and functional properties. Sensory modalities and qualities. Specificity of sensory receptors. Adequate stimulus

16. **Sensory transduction:** Ionic and electrical phenomena in sensory receptors. The process of sensory transduction. Mechanisms of transduction. Generator potential of receptors. The relationship between intensity and frequency of receptor discharge. Adaptation and fatigue. Modulation of sensory receptor activity.
17. **The somatovisceral system:** Cutaneous mechanoreceptors and thermoreceptors. Proprioceptors. Nociceptors. Modalities and sensory qualities of the different types of sensitivity. Functional characteristics of somatosensory receptors. Internal chemoreceptors.
18. **Transmission of the different types of somatovisceral sensations:** the two sensory pathways for transmission of signals to the central nervous system: the dorsal lemniscal system and anterolateral system. Medullary integration. Thalamic integration. Projection to the sensory areas of the cortex. Medullary and supramedullary control of sensory information. Control of pain sensitivity: concept of analgesia: Clinical anomalies of pain and other somatic sensations.
19. **The organ of vision:** General structure of the eye. Ocular muscles. The fibrous tunic: sclerotic. The cornea. The vascular tunic or uvea. The crystalline lens. The vitreous body. The retina: cellular organization of the retina. The pigment epithelium. Photoreceptor cells. Horizontal cells. Bipolar cells. External plexiform layer. Amacrine cells. Interplexiform cells. Internal plexiform layer. Optic nerve fibres. The internal limiting membrane. Neuroglial elements of the retina. Central area and fovea. Blood and lymphatic irrigation of the eye. Nerves in the eye. Accessory organs of the eye: the eyelid and lacrimal gland. Histogenesis of the eye.
20. **The organ of vision:** Physiology of the eye. The creation of images on the retina. Ametropia and correction. Physiology of the cornea and sclerotic. The crystalline lens: generation of cataracts. Physiology of the uvea: the choroid. The ciliary body: ciliary processes and the production and absorption of aqueous humour. Glaucoma.
21. **The organ of vision:** Photochemistry of vision. Visual cycle and excitation of rods. Phototransduction cascade: structural and functional characteristics of rhodopsin, transducin and cyclic nucleotides. Structural characteristics and functions of photosensitive pigments of retinal cones. Vitamin A and photosensitive pigments.
22. **The organ of vision:** Physiology of the retina: Nerve circuits of the retina. Ganglion cells. Excitation of ganglion cells. Functional characteristics of the fovea. Geniculocortical pathway: the primary visual cortex: functional organization. Extrastriate cortical visual areas: functional organization. Parvocellular and magnocellular systems. Representation of the field of vision. Extrageniculate pathway:
Binocular vision. Colour vision. Pupillary pathway: the iris. The photomotor reflex. Pharmacology of the pupil. Eye movements.
23. **The organs of Hearing and Balance:** General structure of the ear. The outer ear. The middle ear: the ear drum and auditory tube. The inner ear. The osseous labyrinth: vestibule and cochlea.
The membranous labyrinth: the utricle, saccule and ampulla. The endolymphatic sac. The cochlear duct. The organ of Corti. The perilymphatic labyrinth. Blood irrigation and innervation in the labyrinth. The auditory nerve and vestibular nerve.
24. **The organ of hearing:** Transmission of sound in the ear. The audible spectrum. Function of sensory cells in the organ of Corti. Endocochlear potential. Cochlear microphonic potentials.
Physiology of the auditory pathway. The auditory thalamus. The auditory cortex. Action potentials of the auditory pathways. Measure of sensitivity. Audiometry. Hearing alterations.
25. **The organ of balance:** Physiology of the vestibular system. Molecular bases of receptors in the semicircular canals, utricle and saccule. Systems of transduction. Functional organization of the vestibular pathways. Electrical activity of vestibular neurons. Vestibular reflexes. Effects of gravity and acceleration. Thermal stimulation. Control of posture and balance: vestibular sensations and control of the cerebellum with the spinal medulla and brainstem. Vertigo.
26. **Sense of taste:** Taste structures: the tongue. Topographical distribution of taste receptors. Taste buds. Taste buds. Innervation.
27. **Sense of taste:** Chemical perception of taste: Molecular bases of taste receptors and transduction systems. Primary sensations. Taste threshold.
28. **Sense of taste:** Function of sensory taste receptors. Basic taste sensations. Factors that affect the intensity of taste sensation. Transmission of taste sensations. Central processing of taste sensations. Role of the sense of taste:
29. **Sense of smell:** The nasal mucosa. The olfactory membrane. Olfactory receptors. The olfactory bulb.
30. **Sense of smell:** Chemical perception of smell: Chemical stimulation of receptors. Molecular bases of olfactory receptors and transduction systems. Odour-binding proteins. Primary sensations of smell. Odour threshold.

31. **Sense of smell:** Function of olfactory receptors. Basic sensations of smell. Factors that affect the intensity of olfactory sensation. Transmission of olfactory signals to the olfactory bulb. Electrical activity of olfactory nerves and tracts. Signal transduction. Olfactory discrimination. Adaptation. The act of smelling. Phenomena related to smell: sneezing, lacrimal secretion, inspiratory inhibition. Vomiting.

VI. ORGANIZATION AND FUNCTION OF THE MOTOR SYSTEM

32. **Microscopic organization of the spinal medulla.** The spinal medulla: general organization. Grey matter and white matter. Lamination. Rachidian ganglia. Somatic efferent radicular neurons. Visceral efferent neurons. Posterior horn neurons. Anterior horn neurons. Arrangement of nerve fascicles. Neurotransmitters in the spinal medulla. Diseases that affect the spinal medulla.
33. **Functional organization of the motor system.** Sensory information and motor control. Effectors in the motor system: Hierarchical levels of motor control. Functional role of the different levels. Integration of peripheral and central afferences. Spinal medulla. Motor systems of the brain stem. Motor cortex activity: direct and indirect control of movement.
34. **Motor functions of the spinal medulla.** Reflexes. Reflex arcs. General characteristics of the reflexes. Classification of reflexes. Muscle tone. Symptomatology of motor damage by medullary section: medullary shock.
35. **Microscopic organization of the brain stem.** Cranial nerves. The reticular formation. Neurotransmitters in the brain stem and particularly in the reticular formation. Diseases that affect the brain stem.
36. **Motor functions of the brain stem, reticular formation and cerebral cortex:** Role of the brain stem in the control of motor function. Functions of specific brain stem nuclei in the control of subconscious stereotypical movements. Integration of the sensory and motor systems. Functions of the motor cortex and corticospinal tract. Motor alterations caused by damage to the brain stem.
37. **Microscopic organization of the cerebellum:** internal structure of the cerebellum. The cerebellar cortex. General structure in layers: Purkinje cells, cerebellar grains, outer stellate cells, basket cells, Golgi cells. Climbing and mossy afferent fibres. Synaptic organization: the cerebellar circuit. Neurotransmitters in the cerebellum.
38. **Motor functions of the cerebellum.** Neural circuit in the cerebellum. Overall function of the cerebellum in the control of movement. Function of the cerebellum in the control of voluntary muscles. Diseases that affect the cerebellum.
39. **Microscopic organization of the basal ganglia and associated nuclei.** Sensory and motor connections. Neurotransmitters in the basal ganglia and associated nuclei.
40. **Motor functions of the basal ganglia.** Diseases that affect the basal ganglia and associated nuclei.

VII. ORGANIZATION AND FUNCTION OF THE LIMBIC AND AUTONOMIC SYSTEMS

41. **Microscopic organization of the diencephalon:** the thalamus. The ventral thalamus. Thalamocortical interactions. The epithalamus: the pineal gland. The hypothalamus. Optic pathways and auditory pathways. Neurotransmitters in the diencephalon. Diseases that affect the diencephalon.
42. **Physiology of the hypothalamus and the limbic system.** Brain activation-stimulation systems. The hypothalamus, a principal efferent pathway of the limbic system. Specific functions of other parts of the limbic system. The amygdala. The hippocampus and limbic cortex. Homeostasis and emotional behaviour.
43. **Functional organization of the autonomic nervous system.** Organization of the nervous system. Basic characteristics of sympathetic and parasympathetic functions. Drugs that stimulate or block sympathetic and parasympathetic neurons.

VIII. ORGANIZATION AND FUNCTION OF THE COGNITIVE SYSTEM

44. **Microscopic organization of the cerebral cortex:** constituent elements. Organization in layers. Cytoarchitecture of cortical neurons. Afferent and efferent nerve fibres. The cortical areas. Organizational models of the cortex. Neural maps. Development of the visual system and auditory system. Neurotransmitters in the cerebral cortex.
45. **Superior functions of the cerebral cortex.** Functions of specific cortical areas. Function of the brain in communication. Intellectual functions of the brain. Function of the corpus callosum and the anterior commissure in the transfer of thoughts, memories, knowledge and other information from one hemisphere to the other. Thought, conscience and memory.

46. **Physiology of wakefulness and sleep:** Biological rhythms. Polysomnography. Sleep-wake cycle: general aspects, mechanisms, sleep and dreams, functions of sleep. Electroencephalogram: evoked potentials.

IX. REGENERATION AND PLASTICITY IN THE NERVOUS SYSTEM

47. **Axonal growth during development.** Cell adhesion molecules. Cell adhesion. Regulation of growth cones. Biochemical properties of axonal growth. Axon regeneration.
Neurotrophic factors: Types and actions. Trk receptors for neurotrophins. Action of steroid hormones in the development of the nervous system. Neurogenesis in adults.
48. **Synaptic plasticity:** Formation, maintenance and plasticity of chemical synapses. Synaptogenesis during development. Reordering of synaptic contacts. Synaptic plasticity in the adult nervous system:
Short-term synaptic plasticity. Long-term potentiation. Molecular basis of long-term potentiation. Long-term depression. Cortical plasticity.

Practical training

1. Microscopic observation of structures of the nervous system, the skin and the sense organs.
2. Histochemical localization of acetylcholinesterase activity
3. Determination of response time to stimuli
4. Recording action potentials and nerve conduction.
5. Sensory discrimination of touch and exploration of the proprioceptive system.
6. Image formation in the normal eye.
7. Determination of the auditory threshold for different frequencies.
8. Exploration of the vestibular system.
9. Electrooculogram
10. Clinical exploration of reflexes
11. Study of myotatic reflex
12. Recording EEG

Neurochemistry seminars

1. NEURON software
2. Excitotoxicity and neurodegeneration (1)
3. Excitotoxicity and neurodegeneration (2)
4. Brain aging
5. Mitochondrial DNA diseases

TEACHING METHODOLOGIES AND LEARNING RESOURCES

Theory classes.

Practical laboratory work.

Functional explorations.

Seminars.

Audiovisual material: Video projections, interactive computer software.